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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,913	12/17/2001	Peter Beyer		5922

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SYNGENTA BIOTECHNOLOGY, INC.
PATENT DEPARTMENT
3054 CORNWALLIS ROAD
P.O. BOX 12257
RESEARCH TRIANGLE PARK, NC 27709-2257

EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,913	BEYER ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16 and 31-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16 and 31-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Rejection of claims 1-23 under 35 U.S.C. 112, first paragraph, written description, requirement is withdrawn in view of Applicant's amendment and arguments.

Rejection of claims 1-23 under 35 U.S.C. 103(a) is withdrawn in view of Applicant's amendment.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-15 and 17-30 are cancelled. Claims 16 and 31-59 are pending and examined.

Claim Objections

Claim 32 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 32 recites that the phyotene desaturase is derived from the *CrtI* gene of *Erwinia uredovora* as does Claim 31.

Claim Rejections - 35 USC § 112

Claims 53-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims drawn to methods of transforming plant cells and plants with expression cassettes comprising nucleotide sequences encoding a bacterial phytoene synthase and a bacterial phytoene desaturase; or a bacterial phytoene synthase, a plant phytoene desaturase, and a plant zeta carotene desaturase; and transformed plant cells and plants thereof; does not reasonably provide enablement for claims drawn to expression cassettes comprising nucleotide sequences encoding phytoene synthase and phytoene desaturase from fungi. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 7/29/2004. Applicant's arguments filed 3/11/2005 have been considered but are not deemed persuasive.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim. Applicant's assertion that claims drawn to fungal sequence have been cancelled and therefore the rejections drawn to the use of fungal sequence is moot is incorrect (response page 13). Claim 53 clearly recites using fungal phytoene desaturase sequences.

The claims are broadly drawn to methods of transforming plants and plant cells with one or more plant expression cassettes capable of directing expression in plant cells of two or three enzymes selected from the group consisting of nucleotide sequences encoding phytoene synthase from bacteria, and phytoene desaturase from bacteria or fungi; phytoene synthase from bacteria, and phytoene desaturase and zeta carotene desaturase from plants and plants comprising said expression cassettes.

Applicants fail to teach polynucleotides encoding phytoene synthase and phytoene desaturase from fungi; or transformed plant cells and plants comprising polynucleotides encoding a phytoene synthase and a phytoene desaturase from fungi together, or in combination with a phytoene synthase polynucleotide from bacteria, wherein the seeds from the transformed plants contain β-carotene (provitamin A) and other carotenoids, and methods of transforming plants and plant cells therewith.

The state-of-the-art is such that one of skill in the art could not predict whether polynucleotides encoding fungal phytoene synthases or phyotene desaturases when isolated and transformed into a plant or plant cell would transcribe a message encoding an active enzyme in a plant or plant cell. The cloning of unexpected cDNA showed that fungal carotenoid genes transcribe mRNA that is alternatively spliced, apparently regulated by cellular conditions, producing either productive or unproductive forms of mRNA. (Lodato P. *et al.*, Applied and Environmental Microbiology, August 2003; Vol. 69, No. 8; pp. 4676-4682; see abstract; and Results beginning on page 4678, column 2 to page 4679 end of column 2). Further, one of skill in the art could not predict that the P domain of the fungal *carRP* gene from *M. circinelloides*, comprising the coding region for both encodes the lycopene cyclase (R domain) and phytoene synthase (P domain), would require the R domain for P domain's phytoene synthase activity and thus, present unexpected problems when attempting to engineer carotenoid biosynthesis in a plant using fungal sequences. (Velayos A. *et al.*, Eur. J. Biochem. 2000, Vol. 267; pp. 5509-5519; see abstract and page 5517, column 2 lines 20-25).

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the

multitude of non-exemplified mRNA sequences, isolating or amplifying non-functional transcripts or isoforms, producing expression vectors and transforming plants therewith, in order to identify those polynucleotides that when expressed, in combination with other heterologous polynucleotides encoding other carotenoid biosynthetic enzymes, result in the production of active fungal phytoene desaturase enzymes or enzyme complexes and plants with increased carotenoids or provitamin A.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the broad scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16, 31-51 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by The Rockefeller Foundation, International Program on Rice Biotechnology; Workshop Report June 10-11, 1993. Potential for Carotenoid Biosynthesis in Rice Endosperm in light of Burkhardt P.K. *et al.* in Rice Genetics III; Proceedings of the Third International Rice Genetics Symposium; Khush G.S. Ed. 1996 (IRRI) International Rice Research Institute, pp.818-820 and in light of Ye X. *et al.* Science, 14 January 2000; Vol. 287, pp. 303-305.

The claims are broadly drawn to a method of producing a plant cell that accumulates carotenoids by transformation with either a plant phytoene synthase and phytoene desaturase or by transformation with a plant phytoene synthase and a *crtI* gene from *Erwinia uredovora* encoding a phytoene desaturase and plant cells and plants transformed thereby.

The Rockefeller Foundation report teaches a method of producing rice plant cells that accumulate carotenoids by transformation with genes encoding a phytoene synthases, a phytoene desaturases and a zeta carotene desaturases from the carotenoid biosynthetic pathways of bacteria, plants and fungi (see pages 3-6 and Appendices C-E); and tobacco transformed with genes from the entire beta-carotene pathway of *Erwinia herbicola* using the 35S CaMv promoter and Rubsco leader/transit sequence that produced orange seeds due to the accumulation of carotenoids (page 3, lines 13-19).

Burkhardt teaches accumulation of levels of phytoene (0.74 μg/g dry weight) in endosperm cells of rice seeds transformed with a gene from daffodil (*Narcissus pseudonarcissus*) encoding a phytoene synthase and a gene from daffodil (*Narcissus pseudonarcissus*) encoding a phytoene desaturase on page 819, lines 27-33 and page 820, the entire paragraph; and that rice endosperm has no carotenoids (i.e. β-carotene and structurally related compounds) on page 819 lines 9-12, and therefore teaches a method of producing plant cells that accumulate carotenoid in endosperm cells of rice plants transformed with a gene encoding a plant phytoene synthase and phytoene desaturase relative to native levels of carotenoid and plants transformed thereby.

Ye teaches transgenic rice plants comprising a polynucleotide encoding a phytoene synthase from a plant (daffodil) and a phytoene desaturase *crtI* gene from *Erwinia uredovora* producing seeds with increased levels of alpha-carotene and betas-carotene in the seed

endosperm relative to native seeds levels on page 304 column 1 1st full paragraph and in column 3 last paragraph and on page 305 in Figure 3; and therefore The Rockefeller reference teaches inherently, a method of producing plant cells that accumulate carotenoid by transformation with a gene from daffodil (*N. pseudonarcissus*) encoding a phytoene synthase and a gene from daffodil (*N. pseudonarcissus*) encoding a phytoene desaturase or by transformation with a gene from daffodil encoding a phytoene synthase and a bacterial *crtI* gene from *Erwinia uredovora* encoding a phytoene desaturase and plant cells and plants transformed thereby; and thus the reference teaches all the limitations of Claims 16, 31-51 and 52.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 53-58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burkhardt P.K. *et al.* in Rice Genetics III; Proceedings of the Third International Rice Genetics Symposium; Khush G.S. Ed. 1996 (IRRI) International Rice Research Institute; pp. 818-820 in view of The Rockefeller Foundation, International Program on Rice Biotechnology; Workshop Report June 10-11, 1993; Potential for Carotenoid Biosynthesis in Rice Endosperm.

The claims are broadly drawn to a method of producing a plant cell that accumulates carotenoids by transformation with either a plant phytoene synthase and phytoene desaturase or by transformation with a plant phytoene synthase and a *crtI* gene from *Erwinia uredovora* encoding a phytoene desaturase and plant cells and plants transformed thereby and a method of

transforming plants and plant cells with one or more plant expression cassettes capable of directing expression in plant cells of two or three enzymes selected from the group consisting of nucleotide sequences encoding a phytoene synthase from bacteria and a phytoene desaturase from bacteria or fungi; or a phytoene synthase from bacteria, and a phytoene desaturase and zeta carotene desaturase from a plant, and plants comprising said expression cassettes.

Burkhardt teaches a method of transforming rice plants (*Liliopsida*) with DNA molecules capable of expressing in plant cells consisting of a phytoene synthase and phytoene desaturase from daffodil, using either the CaMV35S or the endosperm tissue specific rice *Gt1* promoter, and the *hpt* hyrgomycin antibiotic selection gene under control of a constitutive promoter (page 819, lines 27-44); that rice milled endosperm has virtually no beta-carotene (page 818, lines 9-11); the availability of genes encoding the four necessary enzyme activities for carotenoid and beta-carotene biosynthesis in plants and bacteria (page 819, lines 16-22); and the accumulation of high levels of phytoene in the seeds of several lines of transformed rice plants (page 820, lines 1-2).

Burkhardt does not teach transformation using a *crtI* gene from *Erwinia uredovora* encoding a phytoene desaturase or using the plant equivalents of the bacterial *crtI* gene, a combination of a plant phytoene desaturase and zeta carotene desaturase encoding polynucleotides or a transit peptide or *Agrobacterium* mediated transformation.

The Rockefeller Foundation report teaches a method of producing rice plant cells that accumulate carotenoids by transformation with genes encoding a phytoene synthase, a phytoene desaturase and a zeta carotene desaturase from the carotenoid biosynthetic pathways of bacteria, plants and fungi (see pages 3-6 and Appendices C-E); and tobacco transformed with genes from

the entire beta-carotene pathway of *Erwinia herbicola* using the 35S CaMV promoter and Rubsco leader/transit sequence that produced orange seeds due to the accumulation of carotenoids (page 3, lines 13-19).

It would have been obvious at the time of invention to modify the invention of Burkhardt, to substitute for the daffodil phytoene desaturase, the *crtI* polynucleotide encoding the *Erwinia uredova* bacterial phytoene desaturase or the plant phytoene desaturase and zeta carotene desaturase taught by The Rockefeller Foundation report to produce transformed plant cells that accumulate carotenoids. One of skill in the art would have been motivated by the teachings of Burkhardt that the genes encoding the enzymes required for beta-carotene biosynthesis from plants, bacteria and fungi are available in the art, as also taught by The Rockefeller Foundation report, and Applicant's specification; and that rice endosperm contains GGPP the substrate for phytoene synthase, and is thus a valuable tool for engineering provitamin A production, and by the success of Burkhardt in transforming rice with phytoene synthase (daffodil) and phytoene desaturase (daffodil) and producing endosperm cells of rice seeds that accumulated phytoene; that one would have had a reasonable expectation of success in transforming a rice plant cell or plant with a plant phytoene synthase and either a plant phytoene desaturase or bacterial (*crtI*) phytoene desaturase; or a bacterial phytoene synthase and a plant phytoene desaturase and a plant zeta carotene desaturase that would result in the production of a carotenoid or provitamin A in the endosperm cells of a rice seed; and wherein incorporation of transformation using *Agrobacterium tumefaciens* is obvious given the lack of criticality.

Applicant asserts that there is no explanation in the Burkhardt reference as to why there is no accumulation of zeta carotene in rice endosperm cells transformed with the daffodil phytoene desaturase (response page 15). Applicant is arguing limitations that are not found in the claims.

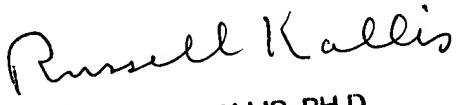
All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
May 19, 2005



RUSSELL P. KALLIS, PH.D.
PATENT EXAMINER